

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 36-37 are pending in the application with claim 36 being the sole independent claim. Claims 36-37 are sought to be amended. Support for the amendment of claim 36 may be found, *inter alia*, at page 11, line 16 to page 12, line 3, Example 1 and Example 3. Claim 37 has been amended to reflect the re-lettering of the steps in claim 36. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Information Disclosure Statement***

The Examiner has acknowledged receipt of the copies of references AR52 and AR67 submitted by Applicants on October 10, 2006, and has requested a listing of these references on a Form PTO-1449. *See* Paper No. 20061204 at page 2. As requested, Applicants enclose copies of pages 52 and 67 of Form PTO-1449 filed on June 10, 2004 listing references AR52 and AR67, respectively. Applicants respectfully request that the Examiner initial references AR52 and AR67 on these forms and indicate in the official file wrapper that these documents have been considered.

***Prior Rejections Under 35 U.S.C. §§ 102 and 103***

Applicants thank the Examiner for reconsidering and withdrawing the rejections of the claims under 35 U.S.C. §§ 102 and 103.

***Claim Objections***

The Examiner has objected to claim 36, requesting that the claim elements be separated by line indentation. *See* Paper No. 20061204 at page 3. As requested, Applicants have amended claim 36 to separate the elements by line indentation. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the objection of claim 36.

***Rejections Under 35 U.S.C. § 112, Second Paragraph - Definiteness***

The Examiner alleges claims 36-37 are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Paper No. 20061204 at page 3. Specifically, the Examiner argues that the phrase "capable of" renders the claim indefinite because it is unclear whether the limitations following the claim are part of the claimed invention. Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, claim 36 has been amended to recite "inhibits" instead of "is capable of inhibiting." Thus, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of the claims.

The Examiner also alleges claim 36 is incomplete for omitting the essential step of obtaining or preparing the A $\beta$  samples. *See* Paper No. 20061204 at pages 3-4. Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, claim 36

has been amended to include the step of obtaining the first and second A $\beta$  samples. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of the claims.

***Rejections Under 35 U.S.C. § 112, First Paragraph - Enablement***

The Examiner has rejected claims 36-37 under 35 U.S.C. § 112, first paragraph, for lack of enablement. *See* Paper No. 20061204 at page 4. According to the Examiner, the specification does not teach any methods or working examples that indicate the administration of a candidate agent *in vivo* would result in the successful treatment of Alzheimer's Disease (AD). *See* Paper No. 20061204 at page 4. The Examiner also argues that *in vitro* experiments do not predict success for the treatment of AD *in vivo* and, as such, it would require undue experimentation for one skilled in the art to practice the invention as claimed. *See* Paper No. 20061204 at page 5. Applicants respectfully disagree for the following reasons.

Claims 36-37 are directed to methods for identifying candidate pharmacological agents to be used in the treatment of AD and/or symptoms thereof. The claimed methods generally involve identifying candidate pharmacological agents that reduce the amount of target protein crosslinking in the presence of a redox-active metal source. As explained in the specification, protein crosslinking mediated by redox-active metals appears to play a prominent role in AD. *See*, generally, Specification at pages 1-4. Accordingly, the method of claim 36 specifies that "an absence of crosslinking in said second sample [comprising a candidate pharmacological agent] as compared to said first

sample indicates that said candidate pharmacological agent has inhibited A $\beta$  crosslinking."

Applicants note that the claims specify that the agent identified by the claimed methods is a *candidate* pharmacological agent identified by an *in vitro* method. The claims do not require that the identified agent necessarily exhibits any particular degree of efficacy in the *in vivo* treatment of AD. Thus, the concerns expressed by the Examiner at pages 5-7 of the Office Action (relating to *in vivo* treatment of AD, toxicity, crossing the blood brain barrier, route of administration, *etc.*) are not relevant to the enablement analysis of the presently claimed screening methods. Accordingly, the *in vitro* results presented in the specification are sufficient to support and enable the claimed methods for identifying candidate pharmacological agents.

Even if it were proper to consider the *in vivo* success of the claimed *in vitro* methods, Applicants respectfully disagree that *in vitro* experiments would not be indicative of *in vivo* success. *In vitro* experimentation is commonly and effectively used to identify candidate agents and such experiments often accurately correlate with *in vivo* biological experiments. In view of the foregoing, Applicants respectfully request that the enablement rejection be reconsidered and withdrawn.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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